

$X_2$  is a hydrophobic residue;  
 $X_3$  is an acidic or an aliphatic residue;  
 $X_4$  is a basic residue;  
 $X_5$  is an apolar residue;  
 $X_6$  is an aromatic residue;  
 $X_7$  is a polar residue;  
 $X_8$  is an aliphatic residue;  
 $X_9$  is an acidic or an aliphatic residue;  
 $X_{10}$  is an aromatic residue;  
 $X_{11}$  is an aromatic residue;  
 $X_{12}$  is a polar residue;  
 $X_{13}$  is Ile;  
 $X_{14}$  is an apolar residue;  
 $X_{15}$  is an acidic residue;  
 $X_{16}$  is a polar residue;  
 $X_{17}$  is a basic or an aliphatic residue;  
 $Z_1$  is  $H_2N-$ ,  $RHN-$  or,  $RRN-$ ;  
 $Z_2$  is  $-C(O)R$ ,  $-C(O)OR$ ,  $-C(O)NHR$ ,  $-C(O)NRR$ ;  
each R is independently ( $C_1-C_6$ ) alkyl, ( $C_1-C_6$ ) alkenyl, ( $C_1-C_6$ ) alkynyl,  
substituted ( $C_1-C_6$ ) alkyl, substituted ( $C_1-C_6$ ) alkenyl or substituted ( $C_1-C_6$ ) alkynyl;  
each “—” between residues  $Z_1$  and  $X_1$  and residues  $Z_2$  and  $X_{17}$  represents a  
covalent linkage; and  
each “—” between residues  $X_1$  through  $X_{17}$  represents a covalent linkage,

wherein the compound reduces cell-associated binding of transferrin as measured in  
an *in vitro* cellular binding assay and produces at least an additive effect with soluble  
HFE $\beta_2m$  heterodimers in reducing cell-associated binding of transferrin as measured in the  
assay.

15. (New) The method of Claim 14, wherein:

$X_1$  is an apolar amino acid;  
 $X_2$  is an aromatic amino acid;

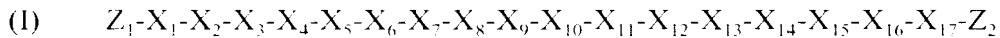
$X_3$  is an acidic amino acid;  
 $X_4$  is a basic amino acid;  
 $X_5$  is an apolar amino acid;  
 $X_6$  is an aromatic amino acid;  
 $X_7$  is a polar amino acid;  
 $X_8$  is an aliphatic amino acid;  
 $X_9$  is an acidic amino acid;  
 $X_{10}$  is an aromatic amino acid;  
 $X_{11}$  is an aromatic amino acid;  
 $X_{12}$  is a polar amino acid;  
 $X_{13}$  is Ile;  
 $X_{14}$  is an apolar amino acid;  
 $X_{15}$  is an acidic amino acid;  
 $X_{16}$  is a polar amino acid;  
 $X_{17}$  is a basic amino acid; and  
each " " between residues  $X_1$  through  $X_{17}$  is independently an amide, a substituted amide or an isostere of amide.

16. (New) The method of Claim 14, wherein:

$X_1$  is Gly;  
 $X_2$  is Trp or Ala;  
 $X_3$  is Asp or Ala;  
 $X_4$  is His;  
 $X_5$  is Met;  
 $X_6$  is Phe;  
 $X_7$  is Thr;  
 $X_8$  is Val;  
 $X_9$  is Asp or Ala;  
 $X_{10}$  is Phe,  
 $X_{11}$  is Trp;  
 $X_{12}$  is Thr;

$X_{13}$  is Ile;  
 $X_{14}$  is Met;  
 $X_{15}$  is Glu;  
 $X_{16}$  is Asn;  
 $X_{17}$  is His or Ala;  
 $Z_1$  is  $H_2N\text{-}$ ;  
 $Z_2$  is  $\text{-C(O)OH}$ ; and  
each "—" between residues  $X_1$  through  $X_{17}$  is an amide linkage.

17. (New) A method of treating an iron overload disease, comprising administering to a subject a therapeutically effective amount of a compound comprising the formula:



wherein:

$X_1$  is an apolar residue;  
 $X_2$  is a hydrophobic residue;  
 $X_3$  is an acidic or an aliphatic residue;  
 $X_4$  is a basic residue;  
 $X_5$  is an apolar residue;  
 $X_6$  is an aromatic residue;  
 $X_7$  is a polar residue;  
 $X_8$  is an aliphatic residue;  
 $X_9$  is an acidic or an aliphatic residue;  
 $X_{10}$  is an aromatic residue;  
 $X_{11}$  is an aromatic residue;

$X_{12}$  is a polar residue;

$X_{13}$  is Ile;

$X_{14}$  is an apolar residue;

$X_{15}$  is an acidic residue;

$X_{16}$  is a polar residue;

$X_{17}$  is a basic or an aliphatic residue;

$Z_1$  is  $H_2N-$ ,  $RHN-$  or,  $RRN-$ ;

$Z_2$  is  $-C(O)R$ ,  $-C(O)OR$ ,  $-C(O)NHR$ ,  $-C(O)NRR$ ;

each R is independently ( $C_1-C_6$ ) alkyl, ( $C_1-C_6$ ) alkenyl, ( $C_1-C_6$ ) alkynyl, substituted ( $C_1-C_6$ ) alkyl, substituted ( $C_1-C_6$ ) alkenyl or substituted ( $C_1-C_6$ ) alkynyl;

each “—” between residues  $Z_1$  and  $X_1$  and residues  $Z_2$  and  $X_{17}$  represents a covalent linkage; and

each “—” between residues  $X_1$  through  $X_{17}$  represents a covalent linkage,

wherein the compound reduces cell-associated binding of transferrin as measured in an *in vitro* cellular binding assay and produces at least an additive effect with soluble HFE/ $\beta_2m$  heterodimers in reducing cell-associated binding of transferrin as measured in the assay.

18. (New) The method of Claim 17, wherein:

$X_1$  is an apolar amino acid;

$X_2$  is an aromatic amino acid;

$X_3$  is an acidic amino acid;

$X_4$  is a basic amino acid;

$X_5$  is an apolar amino acid;

$X_6$  is an aromatic amino acid;  
 $X_7$  is a polar amino acid;  
 $X_8$  is a aliphatic amino acid;  
 $X_9$  is a an acidic amino acid;  
 $X_{10}$  is an aromatic amino acid;  
 $X_{11}$  is an aromatic amino acid;  
 $X_{12}$  is a polar amino acid;  
 $X_{13}$  is Ile;  
 $X_{14}$  is an apolar amino acid;  
 $X_{15}$  is an acidic amino acid;  
 $X_{16}$  is a polar amino acid;  
 $X_{17}$  is a basic amino acid; and  
each “—” between residues  $X_1$  through  $X_{17}$  is independently an amide, a substituted amide or an isostere of amide.

19. (New) The method of Claim 17, wherein:

$X_1$  is Gly;  
 $X_2$  is Trp or Ala;  
 $X_3$  is Asp or Ala;  
 $X_4$  is His;  
 $X_5$  is Met;  
 $X_6$  is Phe;  
 $X_7$  is Thr;  
 $X_8$  is Val;